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Allopurinol Tablets

General Notices

Details for the public consultation of this monograph are as follows:

EAG/Panel/Working Party	Medicinal Chemicals 1
Contact Details	jonathan.campbell@mhra.gov.uk rachael.odubonojo@mhra.gov.uk
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Notes	Revised monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. Identification IR absorption method to replace tests A and B. Dissolution New test added. Related substances Revised disregard and unspecified impurities limits

Action and use

Xanthine oxidase inhibitor; treatment of gout and hyperuricaemia.

DEFINITION

Allopurinol Tablets contain [Allopurinol](#).

The tablets comply with the requirements stated under [Tablets](#) and with the following requirements.

Content of allopurinol, C₅H₄N₄O

95.0% to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of tablets containing 50 mg of Allopurinol in 10 mL of [0.1M sodium hydroxide](#), with the aid of ultrasound, centrifuge and filter (a 0.45-µm filter is suitable). Add 1 mL of [glacial acetic acid](#), allow to stand for 15 minutes. Centrifuge the resulting precipitate, discard the supernatant layer, add

3 mL of [ethanol](#) and mix well. Centrifuge this solution, discard the supernatant layer, and add 4 mL of [diethyl ether](#). Mix and centrifuge this solution, discard the supernatant layer, allow to dry in air for 15 minutes then dry at 105° for 3 hours.

The [infrared absorption spectrum](#) of the residue is concordant with the reference spectrum of allopurinol (RS XXX).

TESTS

Dissolution

Comply with the [dissolution test for tablets and capsules, Appendix XII B1](#).

TEST CONDITIONS

- (a) Use Apparatus 2, rotating the paddle at 75 revolutions per minute.
- (b) Use 900 mL of 0.01M [hydrochloric acid](#), at a temperature of 37°, as the medium.

PROCEDURE

- (1) After 30 minutes withdraw a sample of the medium and filter (a 0.45-µm PVDF/nylon filter is suitable), discarding the first 5 mL of filtrate. Use the filtered medium, diluted with the dissolution medium if necessary to produce a solution expected to contain about 0.0033% w/v of Allopurinol.
- (2) Dissolve [allopurinol BPCRS](#) in a minimum of 0.1M [sodium hydroxide](#) and then dilute the resulting solution to 0.0033% w/v with the dissolution medium.

CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column (15 cm x 4.6 mm) packed with [end-capped octadecylsilyl silica gel for chromatography](#) (5 µm) (XTerra RP-18 is suitable).
- (b) Use isocratic elution and the mobile phase described below.
- (c) Use a flow rate of 0.8 mL per minute.
- (d) Use an ambient column temperature.
- (e) Use a detection wavelength of 250 nm.
- (f) Inject 10 µL of each solution.

MOBILE PHASE

5 volumes of [acetonitrile](#) and 95 volumes of a 0.1M [potassium dihydrogen orthophosphate](#) buffer solution.

DETERMINATION OF CONTENT

Calculate the total content of allopurinol, C₅H₄N₄O, in the medium from the chromatograms obtained and using the declared content of C₅H₄N₄O, in [allopurinol BPCRS](#).

LIMITS

The amount of allopurinol released is not less than 80% (Q) of the stated amount.

Related substances

Carry out the method for [liquid chromatography, Appendix III D](#), using the following solutions prepared in mobile phase A.

- (1) Mix with the aid of ultrasound a quantity of the powdered tablets containing 0.1 g of Allopurinol with 10 mL of 0.1M [sodium hydroxide](#) for about 1 minute, immediately dilute to 200 mL and filter (Whatman GF/C is suitable).
- (2) Dilute 1 volume of solution (1) to 100 volumes, and then to a further 10 volumes.
- (3) 1 volume of 0.05% w/v [allopurinol impurity A BPCRS](#) and 0.025% w/v each of [allopurinol impurity B BPCRS](#), [allopurinol impurity C BPCRS](#), [allopurinol impurity D BPCRS](#) and [allopurinol impurity E BPCRS](#) with 1 volume of solution (1) and diluted to 5 volumes. Dilute 1 volume of the resulting solution to 100 volumes.

CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column (25 cm × 4.6 mm) packed with [end-capped octadecylsilyl silica gel for chromatography](#) (5 µm) (Nucleosil C18 is suitable).
- (b) Use gradient elution and the mobile phase described below.
- (c) Use a flow rate of 1 mL per minute.
- (d) Use an ambient column temperature.
- (e) Use a detection wavelength of 230 nm.
- (f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A 1 volume of [methanol](#) and 9 volumes of 0.125% w/v [potassium dihydrogen orthophosphate](#).

Mobile phase B 3 volumes of [methanol](#) and 7 volumes of 0.125% w/v [potassium dihydrogen orthophosphate](#).

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0 - 30	100 → 0	0 → 100	linear gradient
30 - 40	0	100	isocratic
40-45	100	0	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained from solution (2), the [resolution factor](#) between the peaks due to impurity A and allopurinol is at least 3.0.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to allopurinol (retention time about 8 minutes) are: impurity A, about 0.5; impurities B + C, about 0.8; impurity D, about 3.4 and impurity E, about 3.6.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A is not greater than the area of the corresponding peak in the chromatogram obtained with solution (3) (0.2%);

the area of any unresolved double peak corresponding to impurities B and C is not greater than the area of the corresponding double peak in the chromatogram obtained with solution (3) (0.2%);

the area of any peaks corresponding to impurity D or impurity E is not greater than the area of the corresponding peak in the chromatogram obtained with solution (3) (0.1%);

the area of any other [secondary peak](#) is not greater than 2 times the area of the peak due to allopurinol in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of any other [secondary peaks](#) is not greater than 3 times the area of the peak due to allopurinol in the chromatogram obtained with solution (2) (0.3%).

Disregard any peak with an area less than the peak due to allopurinol in the chromatogram obtained with solution (2) (0.1%).

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Dissolve a quantity of powdered tablets containing 40 mg of Allopurinol with 20 mL of 0.05 M [sodium hydroxide](#) solution. Add 60 mL of mobile phase and mix with the aid of ultrasound. Make up to 100 mL with mobile phase and centrifuge. Dilute 1 volume of the supernatant to 5 volumes with mobile phase to produce a 0.0040% w/v solution of Allopurinol. Filter and discard the first 5 mL of filtrate (a 0.45-µm PVDF/nylon filter is suitable).

(2) 0.0040% w/v of [allopurinol BPCRS](#) in mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used.

DETERMINATION OF CONTENT

Calculate the content of $C_5H_4N_4O$, in the tablets from the chromatograms obtained and using the declared content of $C_5H_4N_4O$ in [allopurinol BPCRS](#).

IMPURITIES

With the exception of impurity F, the impurities limited by the requirements of this monograph include those listed under [Allopurinol](#).